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| **Supplemental Table 1**  Sample Size for Analysis Sub-Groups 2015-2018 |
|  |
|   | Year |  |
| Sub-group | 2015 | 2016 | 2017 | 2018 |  |
|   |   |   |   |   |  |
| **Prescribed Opioid** |   |   |   |   |  |
| Any MME/day | 2,442,294 | 3,066,757 | 2,498,801 | 2,186,699 |  |
| <50 MME/day | 1,981,592 | 2,461,162 | 2,046,370 | 1,854,159 |  |
| 50-89 MME/day | 666,834 | 794,242 | 602,279 | 435,110 |  |
| ≥90 MME/day | 266,210 | 363,349 | 253,704 | 175,955 |  |
|   |   |   |   |   |  |
| **Concurrent Opioid and Benzo** |   |   |   |   |  |
| Any MME/day | 282,342 | 350,826 | 301,918 | 234,252 |  |
| <50 MME/day | 226,383 | 278,269 | 241,925 | 192,438 |  |
| 50-89 MME/day | 80,530 | 95,408 | 77,006 | 51,812 |  |
| ≥90 MME/day | 47,888 | 59,793 | 46,932 | 29,773 |  |
|   |   |   |   |   |  |
| **History** |   |   |   |   |  |
| Substance Use Disorder | - | 550,687 | 514,978 | 567,232 |  |
| Opioid Use Disorder | - | 55,234 | 42,527 | 41,398 |  |
| Overdose | - | 3,576 | 3,028 | 2,621 |  |
| Opioid Use Disorder and Prescribed Opioid | - | 30,825 | 21,968 | 19,475 |  |
| Overdose and Prescribed Opioid | - | 1,164 | 866 | 643 |  |
|   |   |   |   |   |  |
| Source: IBM® MarketScan® commercial claims and encounters database. Notes: Numbers listed are sample sizes for given subgroups used in the analysis. Sample size is not mutually exclusive within years. |  |
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| **Supplemental Table 2**Co-dispensing Naloxone with Opioid Analgesics Among Commercially Insured Individuals with a Recent Diagnosis of Opioid Use Disorder: Rates 2016-2018 |
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|   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |
|   | Naloxone w/ any Opioid |   | Naloxone w/ <50 MME/day Opioid | Naloxone w/ 50-89 MME/day Opioid | Naloxone w/ ≥ 90 MME/day Opioid |
|   |   |
| Demographic-Group | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| All | 11.0 | 12.4 | 27.4\* |   | 6.9 | 7.3 | 19.1\* |   | 10.2 | 12.3 | 27.4\* |   | 17.0 | 20.1 | 42.9\* |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Male | 11.5 | 13.8 | 26.1\* |   | 7.0 | 8.6 | 16.1\* |   | 8.6 | 13.6 | 23.6\* |   | 18.8 | 21.5 | 46.1\* |
| Female | 10.4 | 11.2 | 28.5\* |   | 6.8 | 6.2 | 21.5\* |   | 11.6 | 11.2 | 30.7\* |   | 15.4 | 18.8 | 40.0\* |
| p-value (T-Test) | 0.36 | 0.08 | 0.29 |   | 0.85 | 0.07 | 0.02 |   | 0.13 | 0.38 | 0.10 |   | 0.20 | 0.43 | 0.3 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Age: 0-17 | 0.0 | 35.8 | 0.0 |   | 0.0 | 45.6 | 0.0 |   | 0.0 | 0.0 | 0.0 |   | 0.0 | 0.0 | 0.0 |
| Age: 18-34 | 7.3 | 5.4 | 20.1\* |   | 5.8 | 2.6 | 8.6 |   | 4.7 | 2.6 | 26.9\* |   | 11.5 | 12.6 | 48.9\* |
| Age: 35-44 | 11.5 | 13.8 | 22.6\* |   | 6.7 | 8.9 | 13.9\* |   | 11.2 | 12.0 | 16.9 |   | 18.8 | 18.5 | 38.9\* |
| Age: 45-54 | 11.9 | 12.9 | 28.4\* |   | 6.5 | 6.8 | 20.6\* |   | 11.0 | 15.4 | 35.5\* |   | 18.8 | 20.0 | 35.2\* |
| Age: 55-64 | 11.5 | 13.8 | 31.3\* |   | 8.1 | 8.5 | 24.1\* |   | 11.1 | 13.2 | 26.0\* |   | 16.1 | 23.2 | 49.6\* |
| p-value (Chi-square) | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Northeast | 16.1 | 4.3 | 17.4 |   | 9.8 | 3.0 | 9.8 |   | 18.7 | 3.0 | 10.5 |   | 26.9 | 8.1 | 33.4 |
| Midwest | 4.6 | 8.1 | 22.5\* |   | 1.4 | 4.9 | 14.1\* |   | 4.8 | 8.2 | 30.5\* |   | 9.2 | 7.9 | 38.9\* |
| South | 11.9 | 14.5 | 28.6\* |   | 8.2 | 8.8 | 21.7\* |   | 10.5 | 17.4 | 29.7\* |   | 17.9 | 23.1 | 42.3\* |
| West | 10.1 | 17.6 | 36.4\* |   | 5.9 | 9.2 | 24.8\* |   | 7.7 | 11.6 | 33.1\* |   | 14.3 | 30.7 | 51.6\* |
| p-value (Chi-square) | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |
| *Source: IBM® MarketScan® commercial claims and encounters database Notes:* Estimates are the number of individuals co-dispensed naloxone per 1000 individuals that have received an opioid prescription within the given category and were diagnosed with opioid use disorder less than 90 days before the naloxone rx. All estimates are weighted to be nationally representative for the Commercially Insured Population. Individuals were considered to have been co-dispensed naloxone if an opioid claim and naloxone claim were within 7 days of each other. Estimates are obtained from individuals who were continuously enrolled for the year and the last 90 days of the previous year. T-tests were conducted to examine statistical differences in co-dispensing rates between 2016 and 2018 for each demographic group/morphine milligram equivalent category combination. . Chi-square tests were conducted to examine statistical differences among categorical groups .\* represents that co-dispensing rates were statistically different in 2018 compared to 2016 (p<0.001). |
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| **Supplemental Table 3**Co-dispensing of Naloxone with Opioid Analgesics Among Commercially Insured Individuals with a Recent Opioid Overdose: Rates 2016-2018 |
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|   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |
|   | Naloxone w/ any Opioid |   | Naloxone w/ < 50 MME/day Opioid |  | Naloxone w/ 50-89 MME/day Opioid |   | Naloxone w/ ≥ 90 MME/day Opioid |
|   |   |   |   |
| Demographic-Group | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |   | 2016 | 2017 | 2018 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| All | 8.9 | 25.0 | 33.8\* |   | 2.3 | 20.3 | 22.0\* |   | 13.8 | 19.5 | 34.7 |   | 17.6 | 43.9 | 43.7 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Male | 12.6 | 25.4 | 48.2\* |   | 5.7 | 28.3 | 39.1\* |   | 6.6 | 30.5 | 55.6\* |   | 21.1 | 40.3 | 38.8 |
| Female | 6.4 | 24.7 | 22.8\* |   | 0.0 | 14.4 | 9.3\* |   | 18.9 | 12.2 | 17.7 |   | 15.3 | 46.7 | 47.5 |
| p-value (T-Test) | 0.27 | 0.95 | 0.08 |   | 0.09 | 0.22 | 0.0 |   | 0.34 | 0.30 | 0.15 |   | 0.68 | 0.80 | 0.78 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Age: 0-17 | 0.0 | 0.0 | 0.0 |   | 0.0 | 0.0 | 0.0 |   | 0.0 | 0.0 | 0.0 |   | 0.0 | 0.0 | 0.0 |
| Age: 18-34 | 2.3 | 0.0 | 33.4\* |   | 0.0 | 0.0 | 39.6\* |   | 0.0 | 0.0 | 0.0 |   | 13.7 | 0.0 | 0.0 |
| Age: 35-44 | 0.0 | 53.6 | 33.2\* |   | 0.0 | 67.4 | 31.9\* |   | 0.0 | 60.1 | 24.8 |   | 0.0 | 80.7 | 0.0 |
| Age: 45-54 | 16.4 | 22.1 | 40.3 |   | 5.4 | 13.5 | 15.8 |   | 9.1 | 11.3 | 55.2 |   | 35.3 | 23.3 | 66.7 |
| Age: 55-64 | 12.6 | 31.6 | 30.6 |   | 3.2 | 21.9 | 15.1 |   | 31.9 | 21.5 | 35.1 |   | 13.2 | 53.9 | 47.8 |
| p-value (Chi-square) | <0.001 | <0.001 | 0.5 |   | 0.03 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Northeast | 19.6 | 25.4 | 29.3 |   | 6.5 | 35.8 | 10.6 |   | 21.1 | 83.3 | 0.0 |   | 62.4 | 47.8 | 69.4 |
| Midwest | 0.0 | 0.0 | 23.6\* |   | 0.0 | 0.0 | 5.5 |   | 0.0 | 0.0 | 63.5\* |   | 0.0 | 0.0 | 0.0 |
| South | 16.8 | 31.7 | 29.9 |   | 3.6 | 16.0 | 25.3\* |   | 30.0 | 28.1 | 13.0 |   | 27.9 | 40.9 | 37.2 |
| West | 0.0 | 43.1 | 58.6\* |   | 0.0 | 43.5 | 47.3\* |   | 0.0 | 0.0 | 67.7\* |   | 0.0 | 89.5 | 76.1\* |
| p-value (Chi-square) | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |   | <0.001 | <0.001 | <0.001 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| *Source: IBM® MarketScan® commercial claims and encounters database Notes:* Estimates are the number of individuals co-dispensed naloxone per 1000 individuals that have received an opioid prescription within the given category and were diagnosed with an opioid overdose less than 90 days before the naloxone rx. All estimates are weighted to be nationally representative for the Commercially Insured Population. Individuals were considered to have been co-dispensed naloxone if an opioid claim and naloxone claim were within 7 days of each other. Estimates are obtained from individuals who were continuously enrolled for the year and the last 90 days of the previous year. T-tests were conducted to examine statistical differences in co-dispensing rates between 2016 and 2018 for each demographic group/morphine milligram equivalent category combination. Chi-square tests were conducted to examine statistical differences among categorical groups. \* represents that co-dispensing rates were statistically different in 2018 compared to 2016 (p<0.001) |
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| **Supplemental Table 4** Market Share of Dispensed Naloxone by Region Among the Commercially Insured Population 2015-2018 |
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|   |   |   |   |   |   |   |   |  |
|   |   |   | Market Share by Census Region |  |
| Year | Product | All | Northeast | Midwest | South | West |  |
|   |   |   |   |   |   |   |   |  |
| 2015\* | All (n) | 7,229 | 1,494 | 1,001 | 2,916 | 1,805 |  |
| EVZIO Auto Inj. (%) | 72.0 | 50.0 | 78.5 | 81.7 | 71.5 |  |
| Naloxone HCL (%) | 28.0 | 50.0 | 21.5 | 18.3 | 28.5 |  |
| Narcan Nasal (%) | - | - | - | - | - |  |
|   |   |   |   |   |   |   |   |  |
| 2016\* | All (n) | 36,671 | 8,205 | 4,393 | 15,990 | 8,080 |  |
| EVZIO Auto Inj. (%) | 67.0 | 60.4 | 63.9 | 76.4 | 56.9 |  |
| Naloxone HCL (%) | 13.6 | 21.6 | 14.0 | 8.5 | 15.4 |  |
| Narcan Nasal (%) | 19.4 | 18.0 | 22.2 | 15.1 | 27.8 |  |
|   |   |   |   |   |   |   |   |  |
| 2017\* | All (n) | 49,117 | 8,274 | 7,320 | 22,485 | 11,030 |  |
| EVZIO Auto Inj. (%) | 18.2 | 18.3 | 17.8 | 20.4 | 13.9 |  |
| Naloxone HCL (%) | 10.4 | 9.8 | 8.0 | 10.6 | 11.9 |  |
| Narcan Nasal (%) | 71.3 | 71.7 | 73.9 | 68.8 | 74 |  |
|   |   |   |   |   |   |   |   |  |
| 2018\* | All (n) | 99,917 | 14,962 | 16,318 | 45,046 | 23,591 |  |
| EVZIO Auto Inj. (%) | 5.0 | 3.5 | 6.2 | 6.7 | 1.8 |  |
| Naloxone HCL (%) | 5.5 | 3.6 | 5.4 | 6.4 | 4.9 |  |
| Narcan Nasal (%) | 89.5 | 92.7 | 88.3 | 88.7 | 93.3 |  |
|  |  |
| *Source: IBM® MarketScan® commercial claims and encounters database Notes:* Unknown Region category was excluded from table. \*indicates p<0.001 from Chi-square testing of significant association between product type and region within a given year  |  |
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